According to promising preclinical results published in Nature Medicine and Cancer Cell

Drugs from ORYZON shown to be efficacious in the treatment of Acute Leukemia

Barcelona, April 12th 2012.- Drugs against LSD1 discovered and developed by Oryzon, a Biopharmaceutical company dedicated to the discovery of biomarkers and development of novel therapeutics and diagnostics, have been shown to be effective in the treatment of acute leukemia's. These preclinical findings are reported from two independent groups in UK in the last month issues of **Nature Medicine** and **Cancer Cell**. These promising results open new avenues to treat these cancers.

The researches have been directed by **Dr. Arthur Zelent**, from the Division of Molecular Pathology, at the Institute of Cancer Research, Sutton, UK. and by **Dr. Tim Somervaille**, from the *Cancer Research UK Leukaemia Biology Laboratory* at the prestigious *Paterson Institute for Cancer Research* (Manchester, UK.). This last team carried out its experiments synthesizing LSD1 inhibitors described in Oryzon's patents.

The results obtained are promising as they show that inhibition of the epigenetic target LSD1 (also known as KDM1A) is efficient in the treatment of acute myeloid leukemia which represents 40% of all leukemias in humans and especially an aggressive form of acute myeloid leukemia called mixed lineage leukemia (MLL)

The British researchers concluded that their data point to a significant potential therapeutic window for the use of LSD1 inhibitors in the MLL molecular subtype of AML. In an independent press release form the Cancer Research UK[3] **Dr. Somervaille** said "It's difficult to successfully treat patients with this type of leukaemia. There aren't any targeted drugs available and many patients can't be cured with current treatments, such as intensive chemotherapy and bone marrow transplantation. So there's an urgent need for new drugs. "We're very pleased to have tested molecules that homes in on an enzyme called LSD1 in a completely new approach to stop the growth of this disease. And we also believe this target may be important in a range of other types of cancer, but more research is needed".

Both teams propose that LSD1 inhibitors could be in the future part of the combined therapies that are used to treat these tumors. Thus in the acute promyelocytic leukemia (APML) subtype of AML where all - trans retinoic acid (ATRA) is used to induce remission, combined treatments with LSD1 inhibitors could be beneficial.

Besides these independent reports, internal research done by Oryzon's scientists show that LSD1 inhibition could also be efficacious in the treatment of Acute Lymphoblastic Leukemias (ALLs) that represents 25% of juvenile leukemias.

Dra. Tamara Maes, C.S.O. and co-founder of the company declared "from our preliminary results we are confident that our inhibitors of LSD1 could be brought to clinical trials in leukemias and other kinds of cancer next year"

The reports of these groups and the impact of their results have provoked that the journal **Science Business Exchange** (SciBx), from the makers of Nature and BioCentury, dedicated an analysis to this approach in their issue of April 4th, with comments included from Dra. Tamara Maes, C.S.O. and co-founder of Oryzon. In this analysis the company is described as the most advanced in the development of this type of molecules. In fact, Oryzon is a global leader in LSD1 inhibition. The company has produced about 800 compounds that are protected by 20 patents.

About Oryzon

Founded in 2000, Oryzon (www.oryzon.com) has one of the most complete technological platforms for biomarker identification in Europe. With a strong specialization in genomics, proteomics and bioinformatics, the company identifies biomarkers for a variety of neoplasic and neurodegenerative diseases. The company has a powerful platform for biomarker and target validation which includes technologies such as RNAi, microarrays, phage display and a structural genomic platform with a fragment screening approach (NMR and X ray crystallography). Oryzon develops new drugs and monoclonal antibodies against targets identified in its biomarker discovery programs but also develops diagnostic products.

Recently, the company announced its decision to enter in preclinical development with its first drug candidate, a first-in-class bispecific Lysine Specific Demethylase 1 (LSD1) and Monoamine oxidase B (MAO-B) inhibitor for the treatment of Huntington disease (HD).

GynEC®-DX is a good example of the Diagnostic activity of the company. This product was discovered after 5 years of intense research. It is a signature of 5 genes differentially expressed that are highly accurate to determine cancer status in uterine aspirates and when combined with pathology on aspirates has a Negative predictive value of 99,6% according to the results obtained in a recent multi-centric double blind prospective study. Commercialization of this product that has been developed jointly with Laboratorios Reig-Jofré is expected in 1Q 2012.

Other launches under way

Oryzon entered into a partnership in the field of molecular diagnostics with New Zealand firm Pacific Edge Ltd in 2011. According to the agreement, Oryzon holds an exclusive license to market the Cxbladder assay, which detects bladder cancer in urine in some European countries. Oryzon will run the Cxbladder test in its Clinical Analysis Lab, which was authorized by the Catalonian Government last year. "*The central lab is the axis and launching platform of our diagnostic and personalized medicine division*", explains Carlos Buesa. "*We have shown that our biomarker discovery platform is capable of developing personalized medicine*

products and bringing them to market. The goal is to become the leader in molecular diagnostics in Spain and to partner our therapeutic programs with specialized pharmaceutical companies.

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[2] **Cancer Cell**. 2012 Mar 28. *The Histone Demethylase KDM1A Sustains the Oncogenic Potential of MLL-AF9 Leukemia Stem Cells*. Cancer Research UK Leukaemia Biology Laboratory, Paterson Institute for Cancer Research, University of Manchester, UK.

[3] http://info.cancerresearchuk.org/news/archive/pressrelease/2012-03-19-leukaemia-drug-target?ssSourceSiteId=funding

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